Emerging treatment for hair loss targeting dormant follicles

Arash Mostaghimi MD MPA MPH

Vice Chair of Clinical Trials and Innovation, Brigham & Women's Hospital
Director of Dermatology Inpatient Service, Brigham & Women's Hospital
Associate Professor of Dermatology, Harvard Medical School

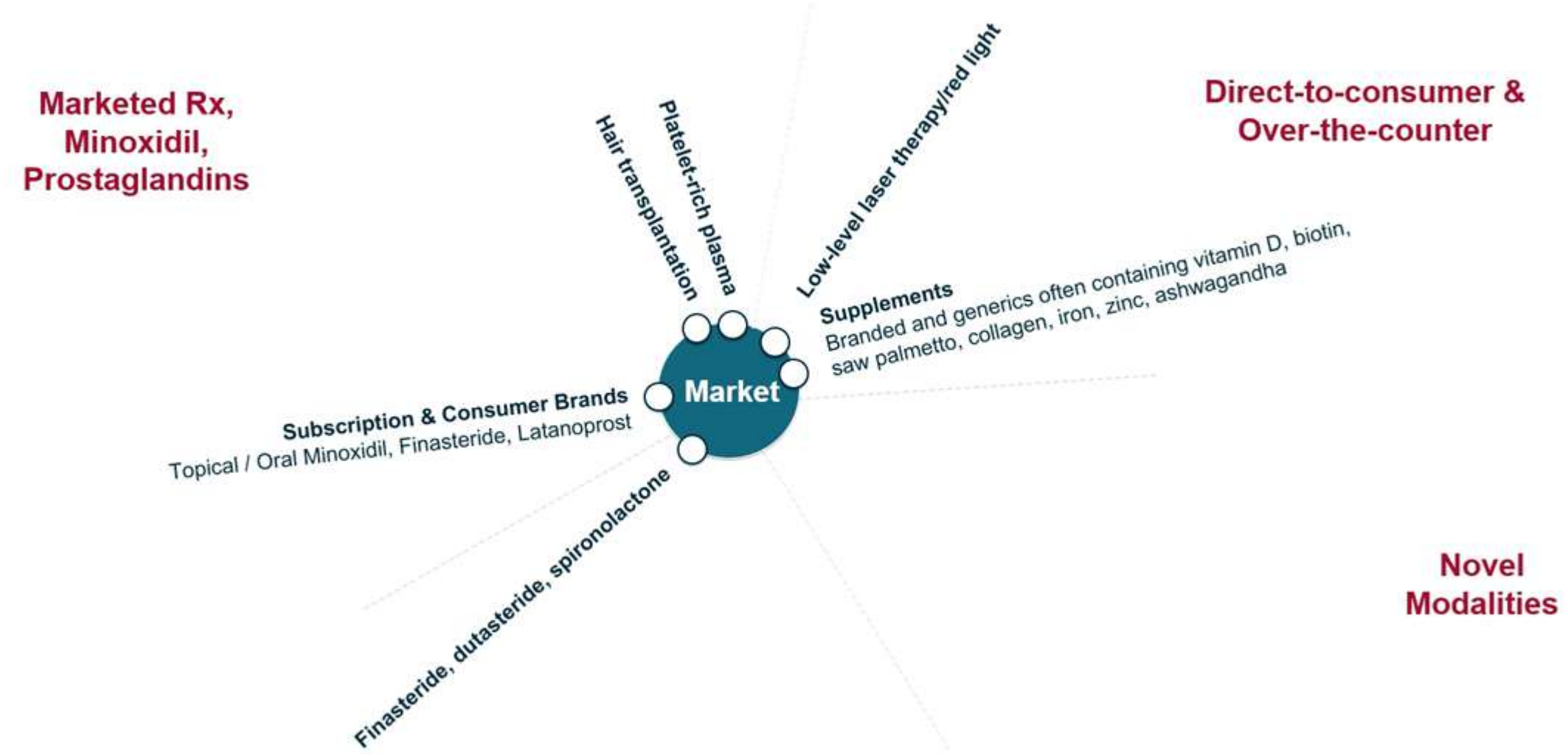
Disclosures

I am a consultant or have led clinical trials for Pfizer, hims and hers, Dermatheory, Digital Diagnostics, AbbVie, Lilly, Sun, Soterios, Legacy Healthcare, Equillium, ASLAN, Q32 Bio, Pelage, and Dren Bio.

I am on the scientific advisory board for Pelage.

We will be discussing off-label indications for medications

The present and future of treatments for androgenetic alopecia (AGA)



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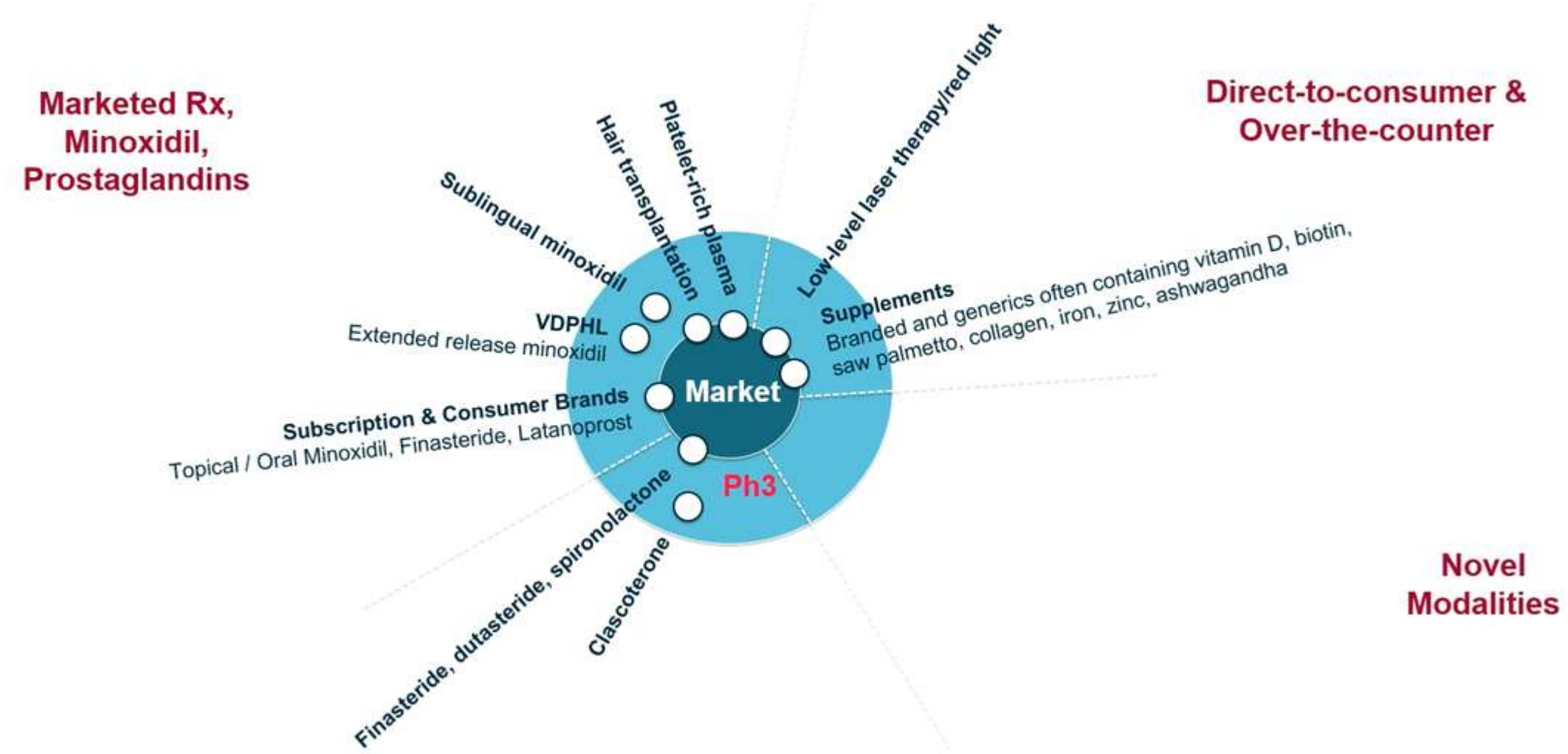

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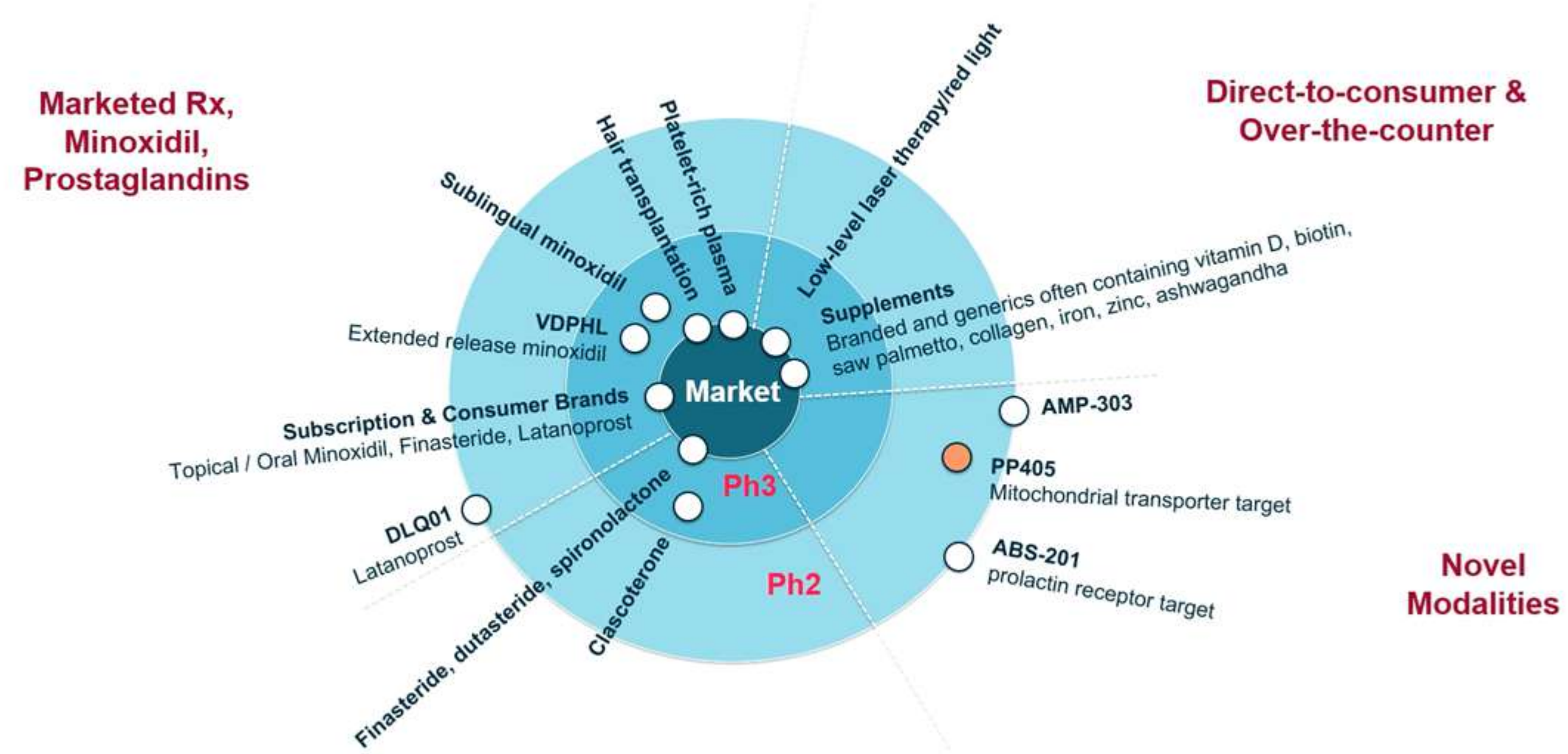

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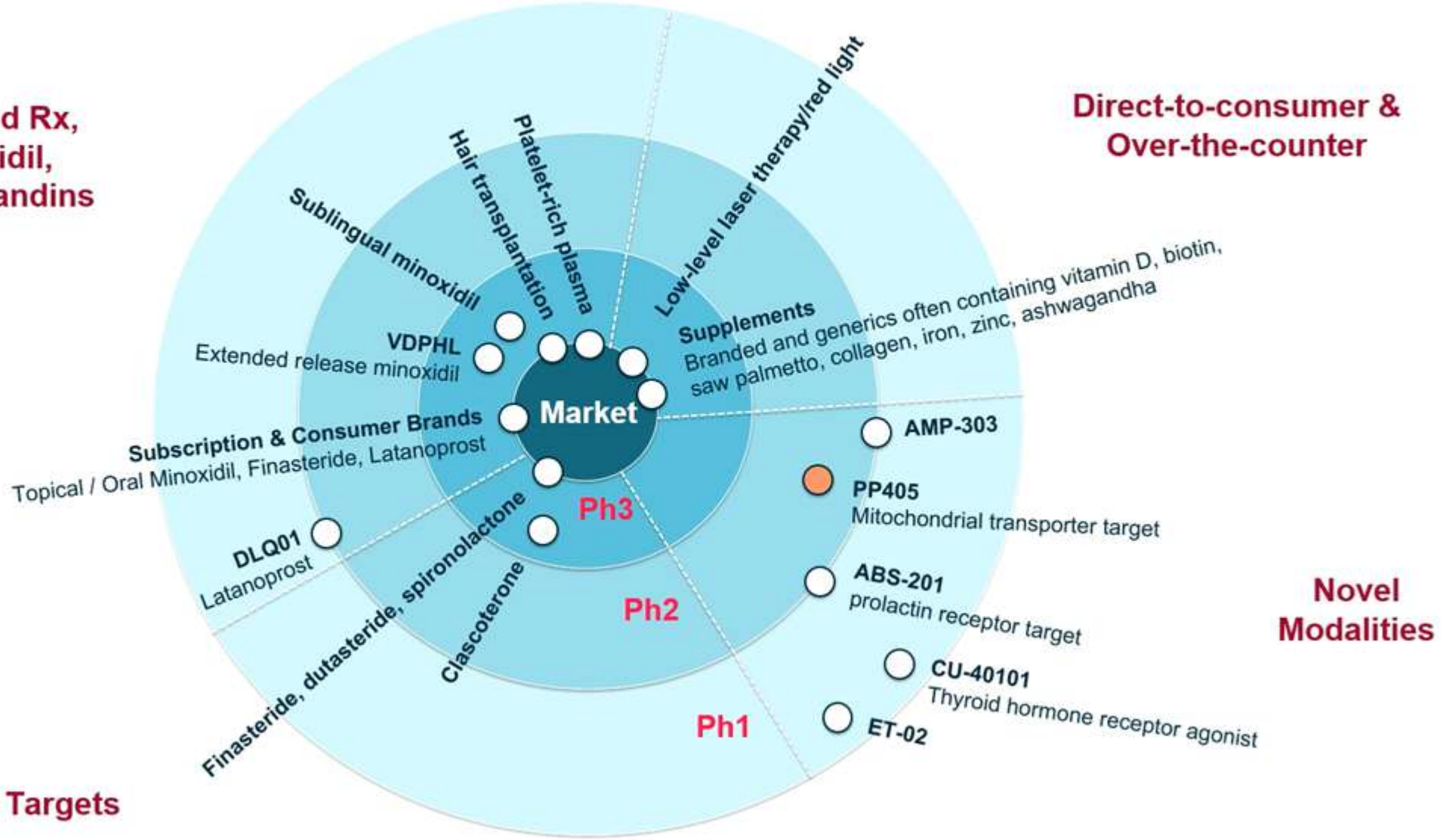

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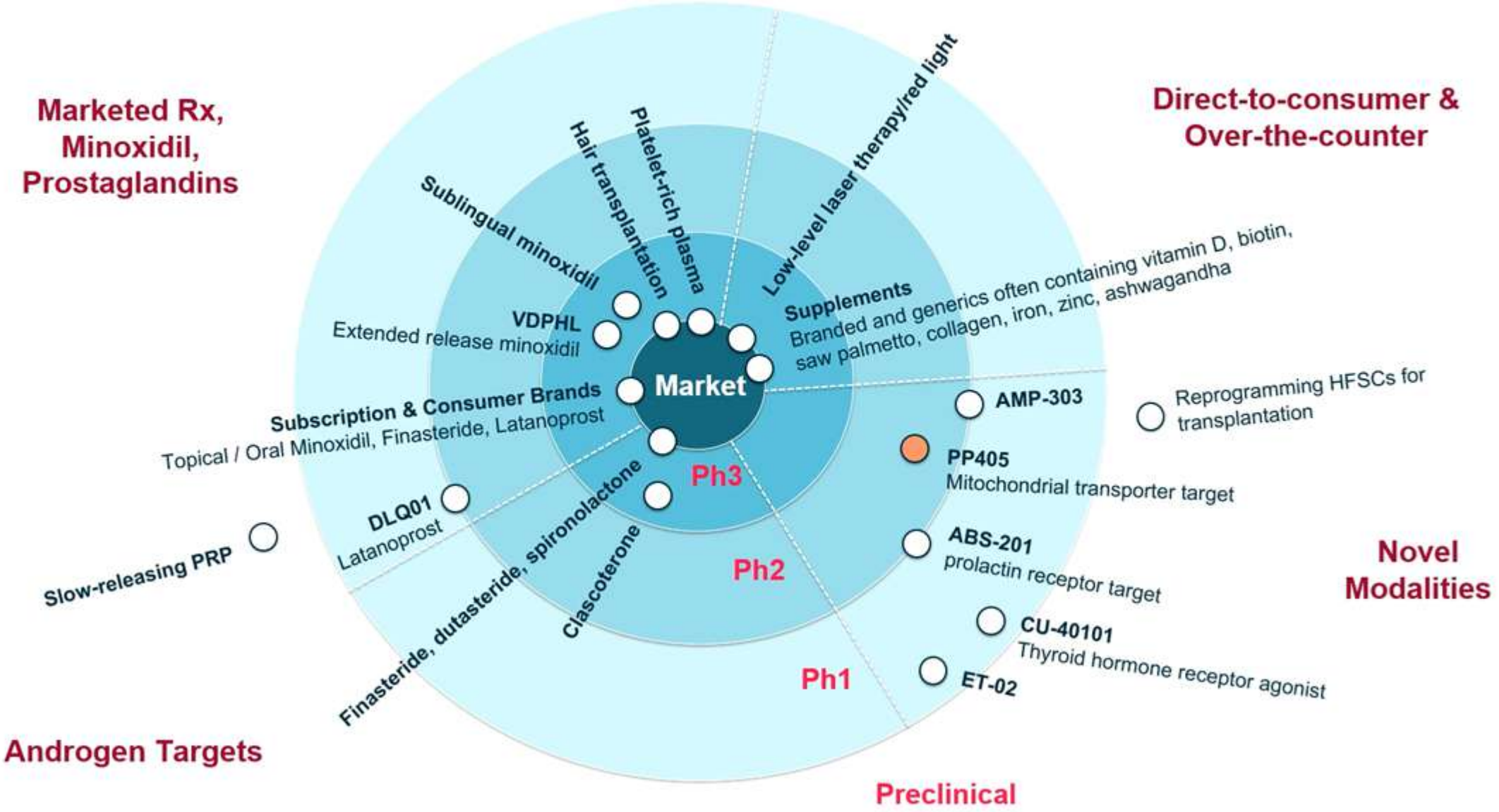


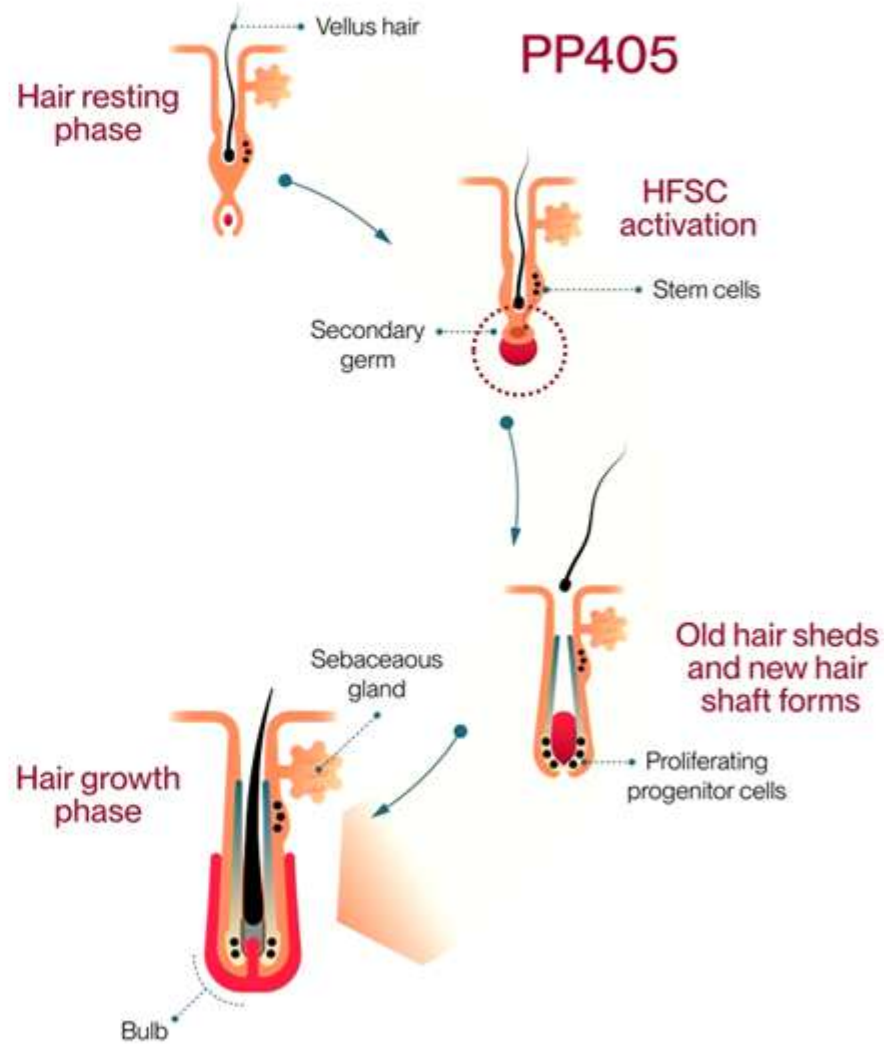
PP405 is a topical small molecule that activates follicular stem cells

Hair Follicle Stem Cells (HFSCs) are quiescent most of the time and permanently reside in the follicle. Balding scalp retains hair follicles and HFSCs.

Activating HFSCs triggers hair growth. HFSC activation stalls over time due to age, stress, genetics, and hormones.

HFSCs are uniquely primed for activation by stimulating Lactate Dehydrogenase (LDH) activity

PP405 inhibits MPC, a mitochondrial transporter, driving LDH activity and activating HFSCs to re-activate dormant follicles and drive hair growth.



How can we improve AGA?

INCREASE TOTAL NUMBER OF HAIRS

- Non-vellus Target Area Hair Count (nvTAHC)
- Non-vellus and vellus TAHC

INCREASE THICKNESS OF THE HAIR

- Terminal-Vellus ratio
- Target Area Hair Width

INCREASE LENGTH OF HAIR

- Hair length
- Rate of hair growth

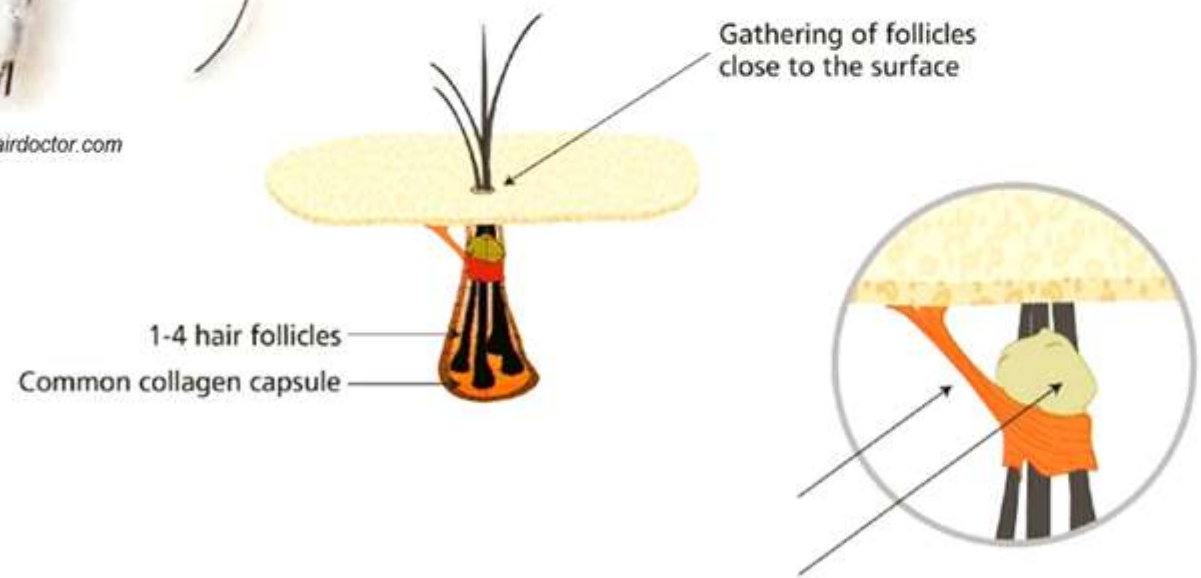
INCREASE NUMBER OF FOLLICULAR UNITS WITH HAIR

- Follicular Unit Count
- Follicular Units with non-vellus hair

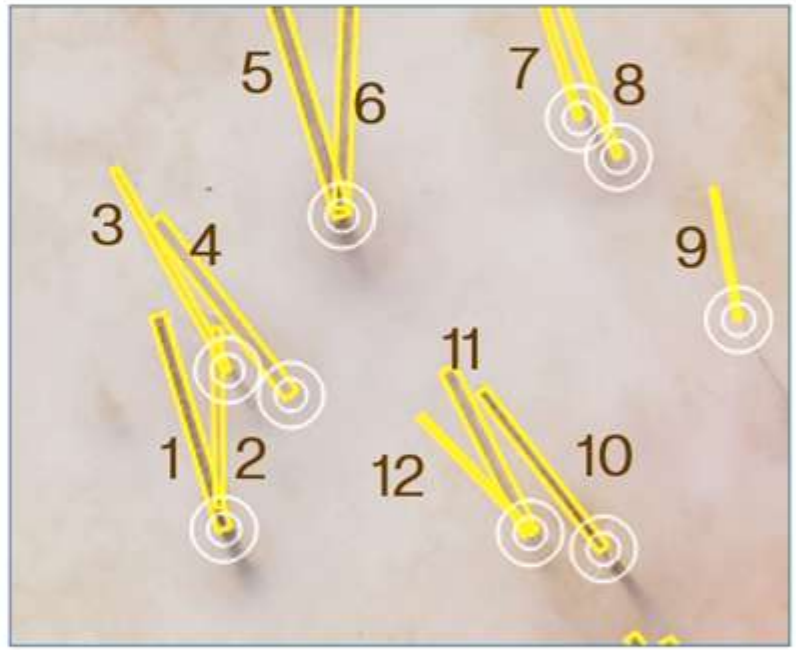
The role of the follicular unit in hair growth

Follicular Unit Count: # follicular orifices with at least one detectable hair shaft

https://nashvillehairdoctor.com



K. Anastassakis, Androgenetic Alopecia From A to Z, https://doi.org/10.1007/978-3-031-10613-2_9



nvTAHC = 12

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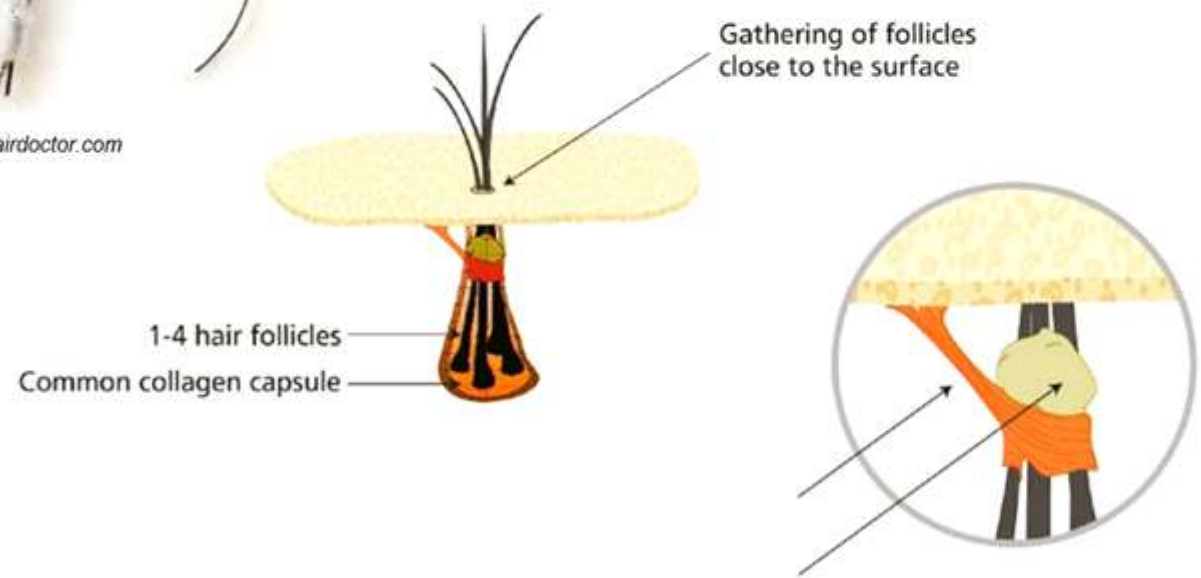

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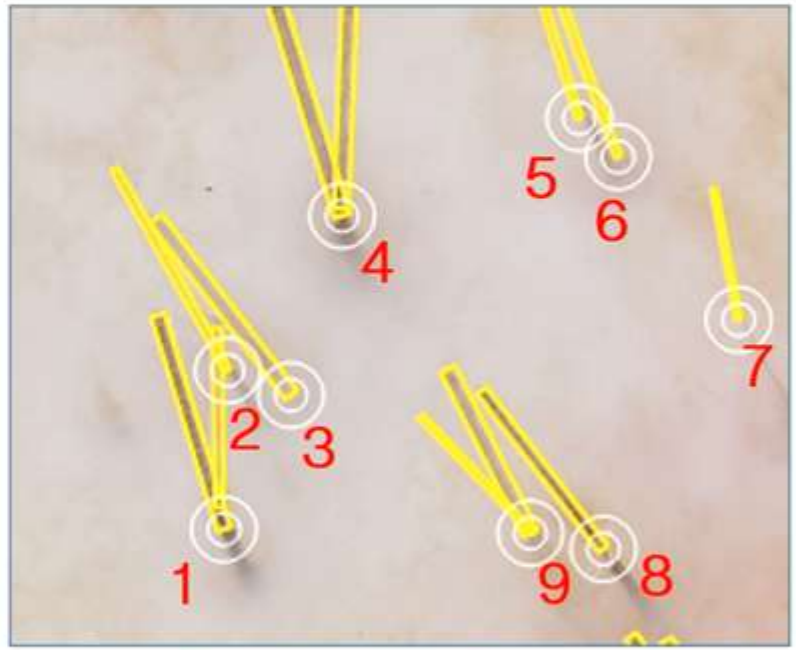
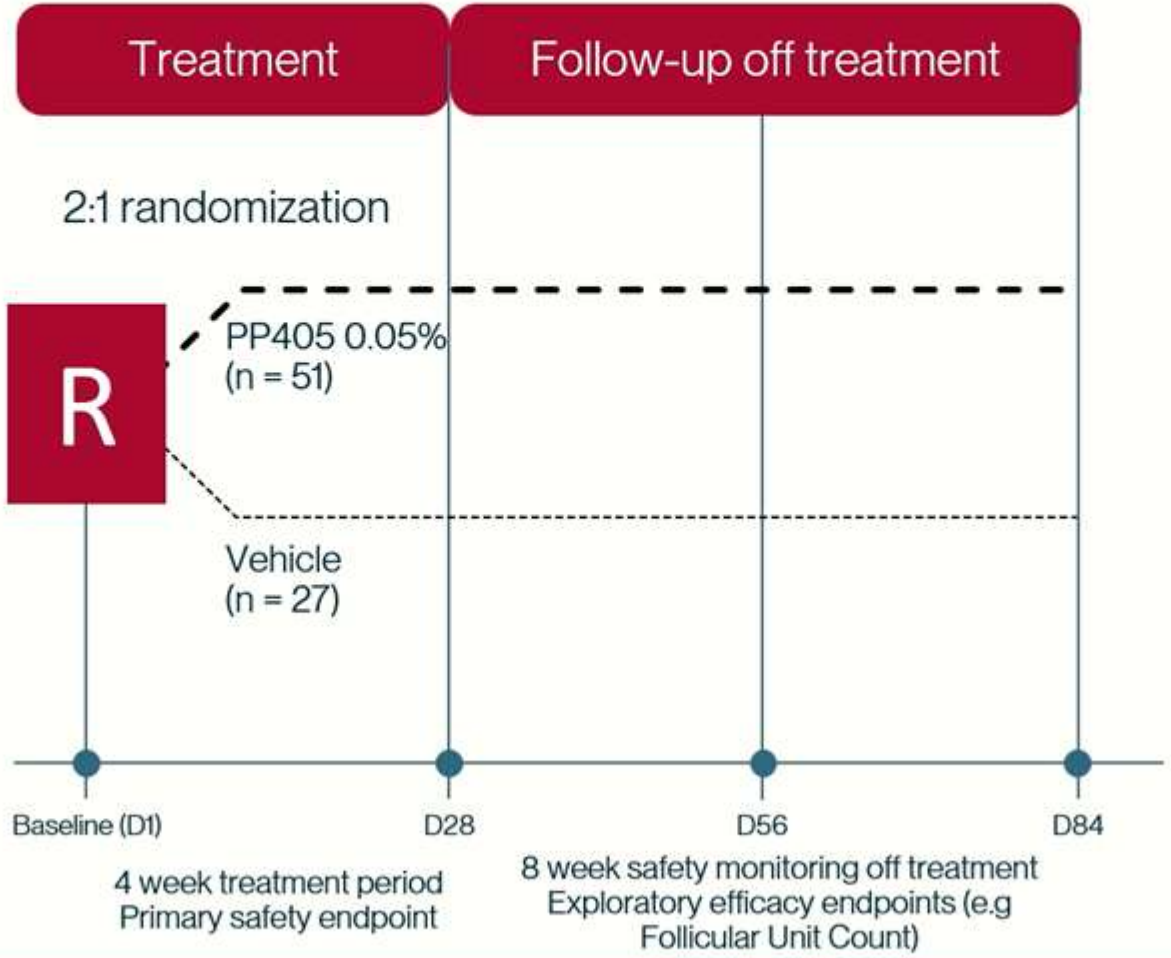


Follicular Unit Count = 9

PP405 Phase 2a study design

RANDOMIZED CONTROL TRIAL WITH OPEN LABEL SAFETY EXTENSION (78 men and women)



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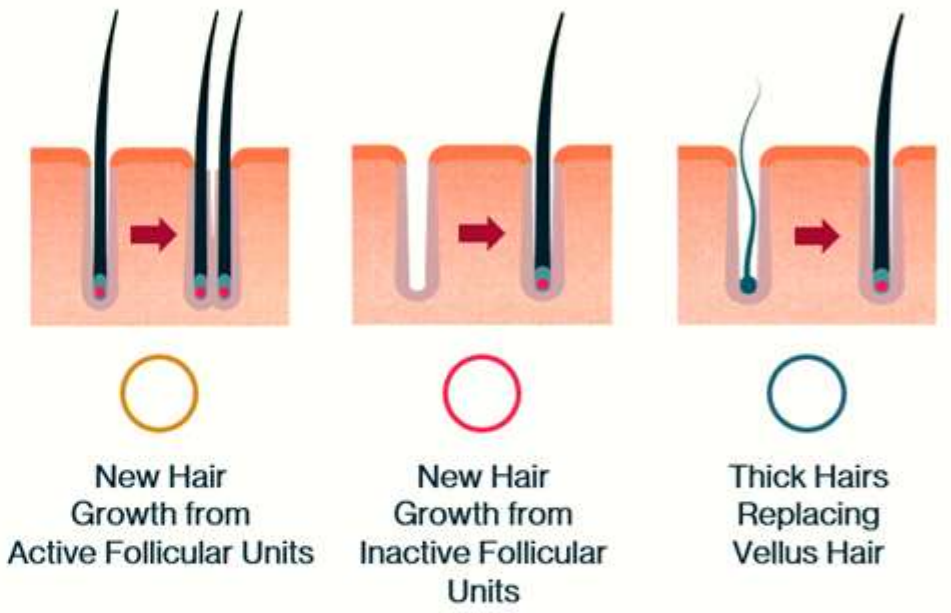
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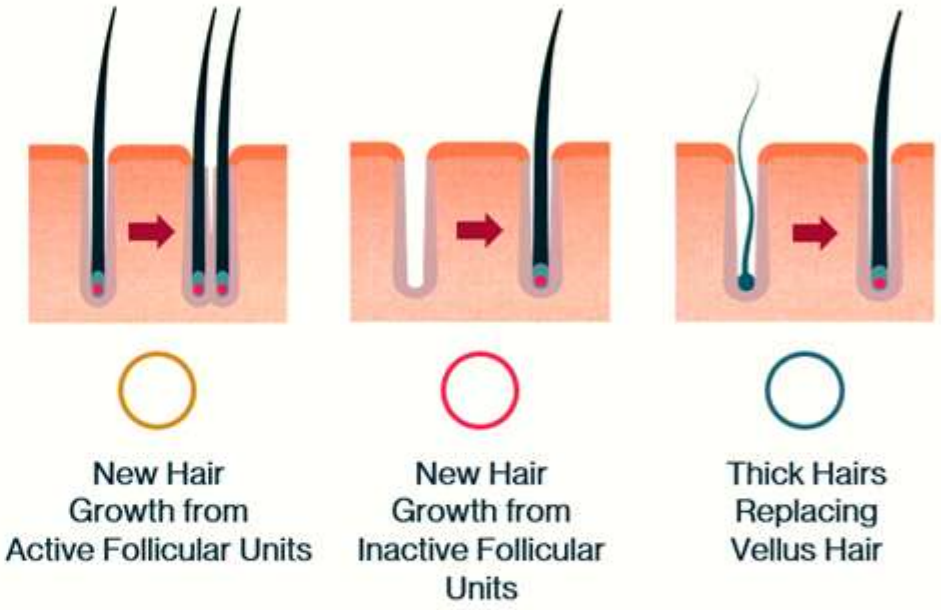
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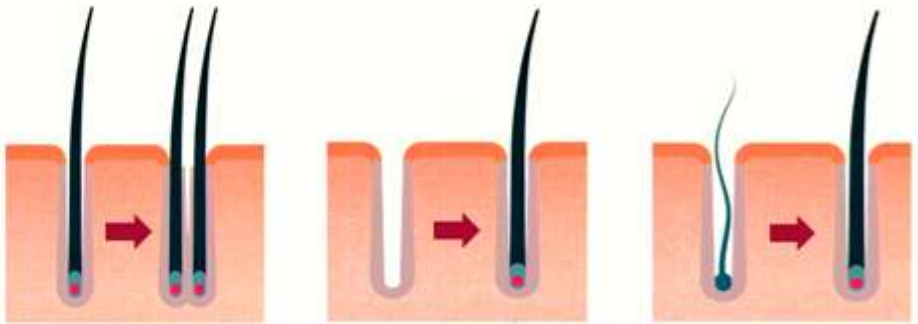

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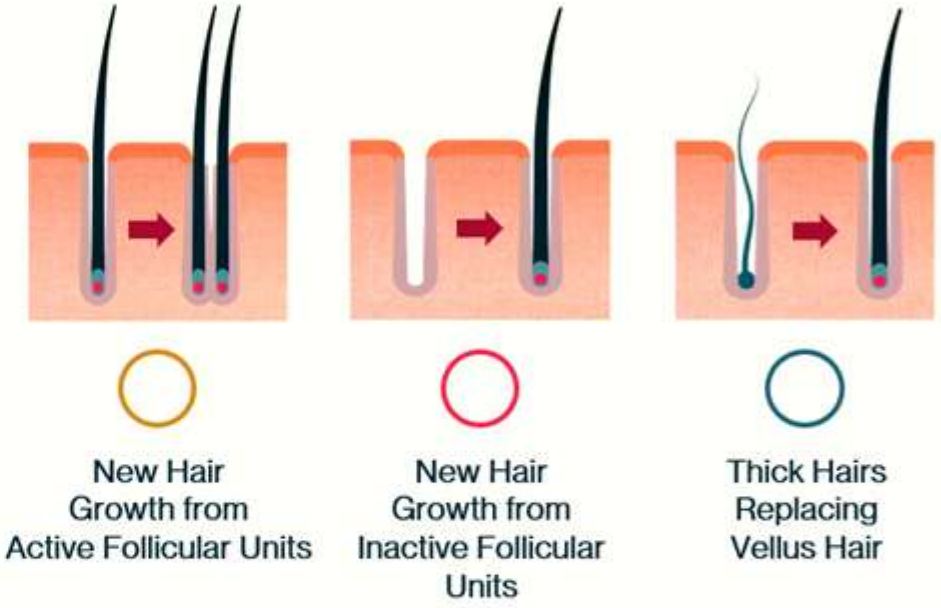
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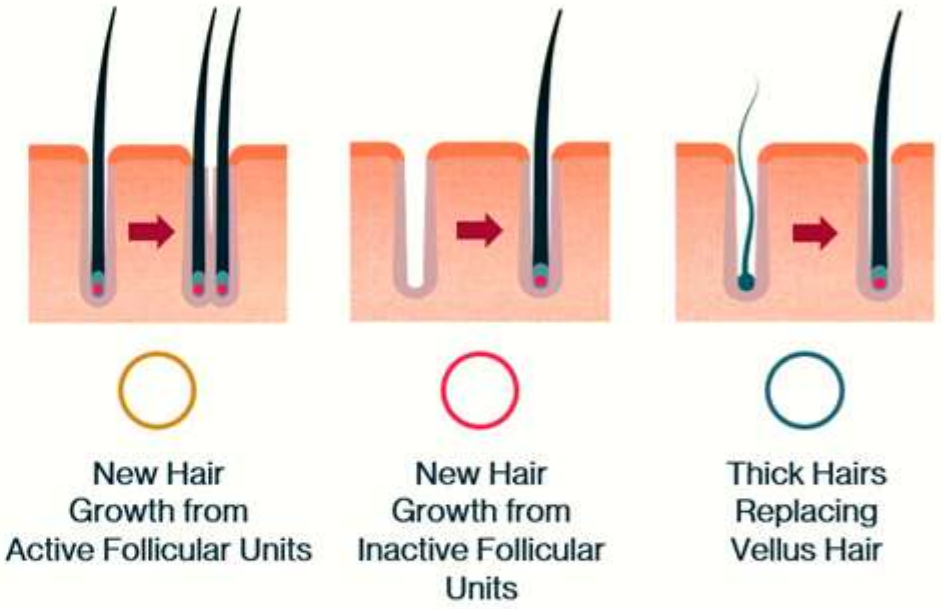
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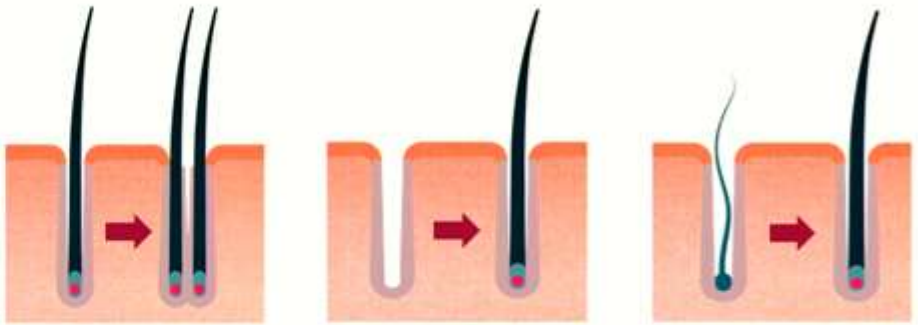

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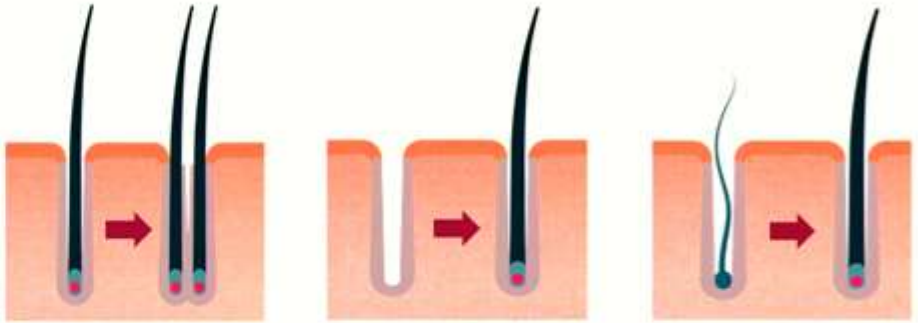

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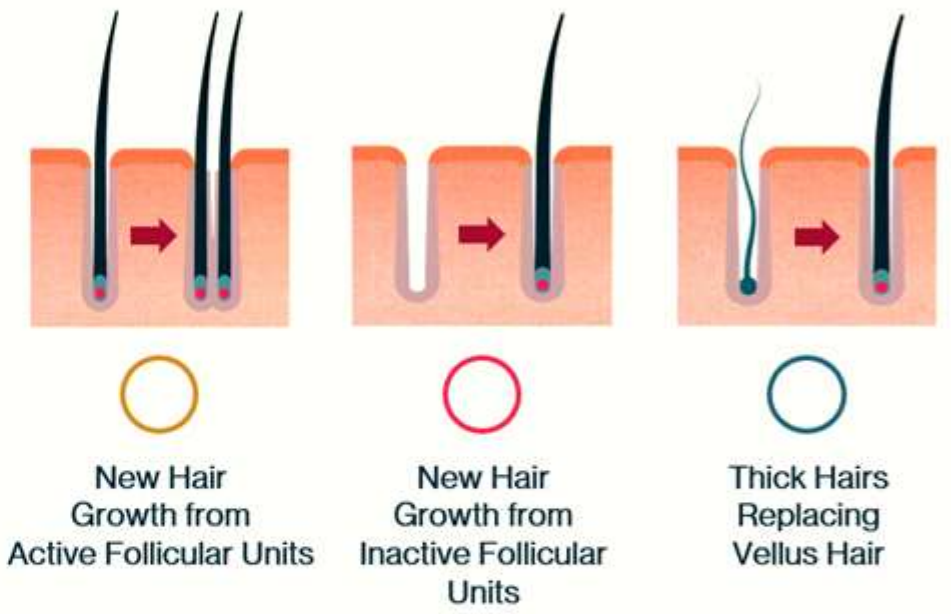
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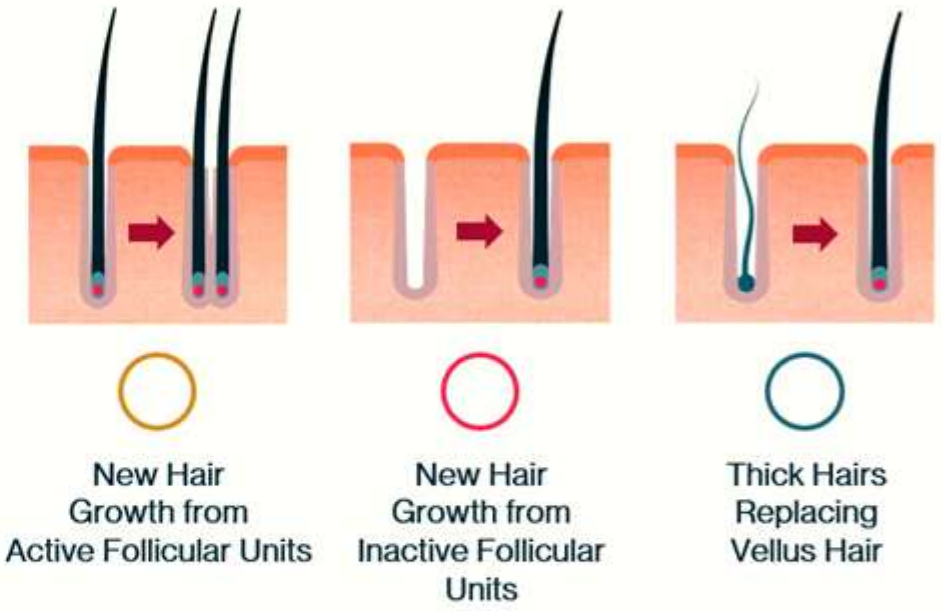
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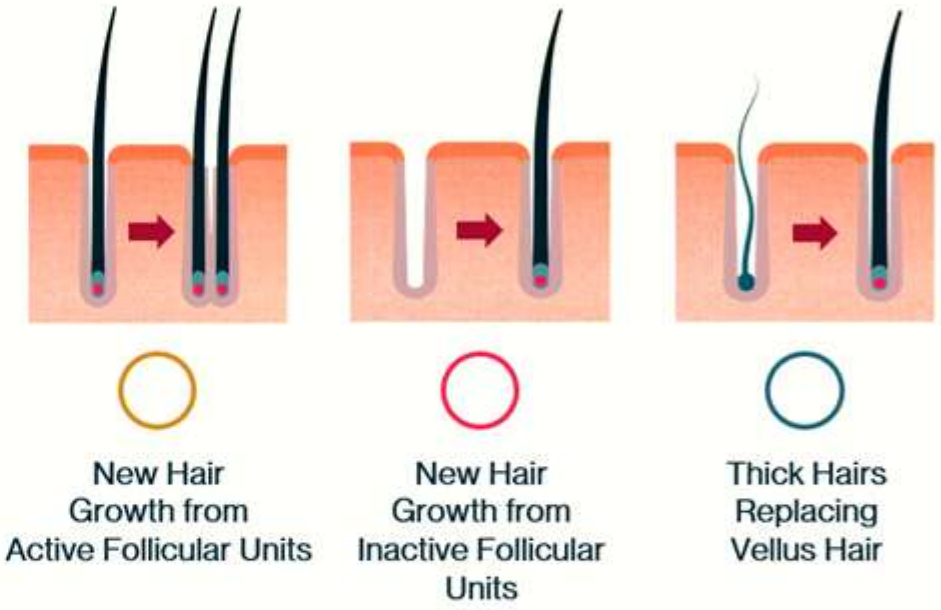
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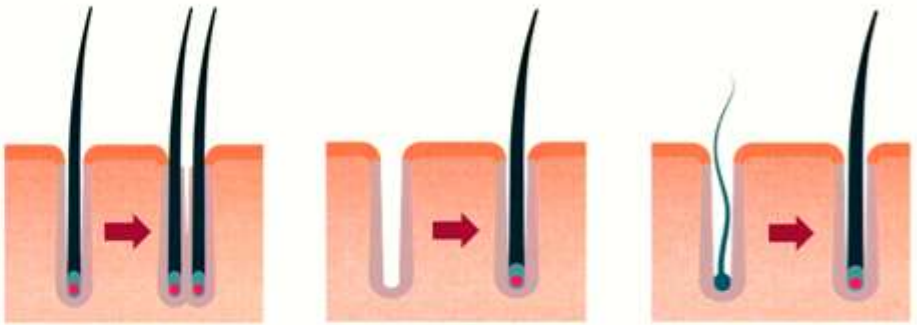
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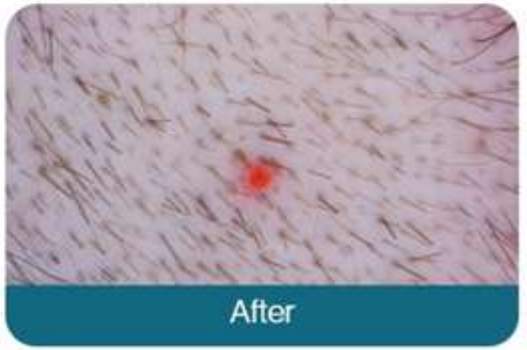

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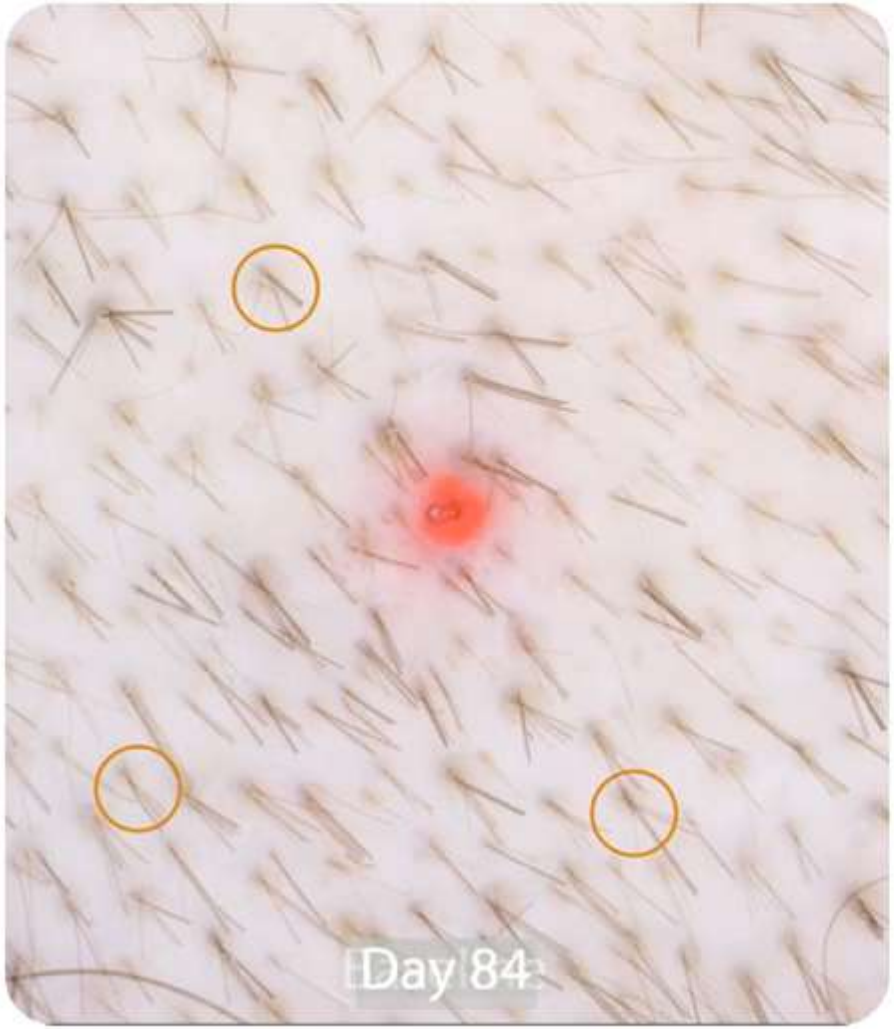

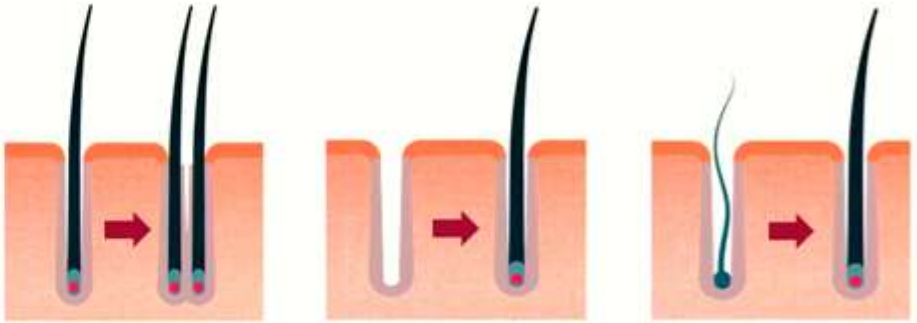

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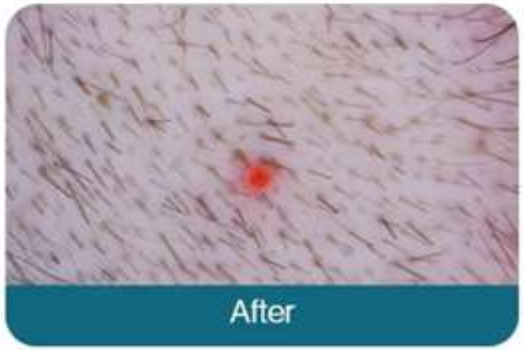

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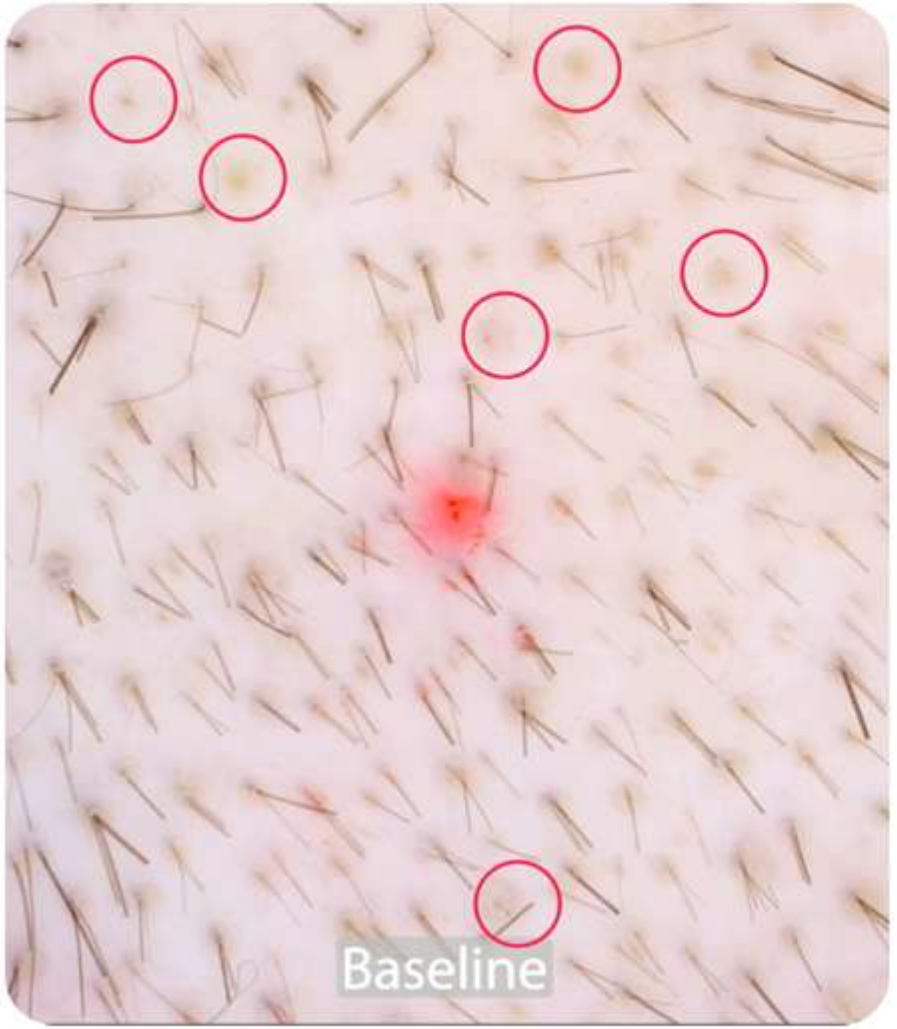

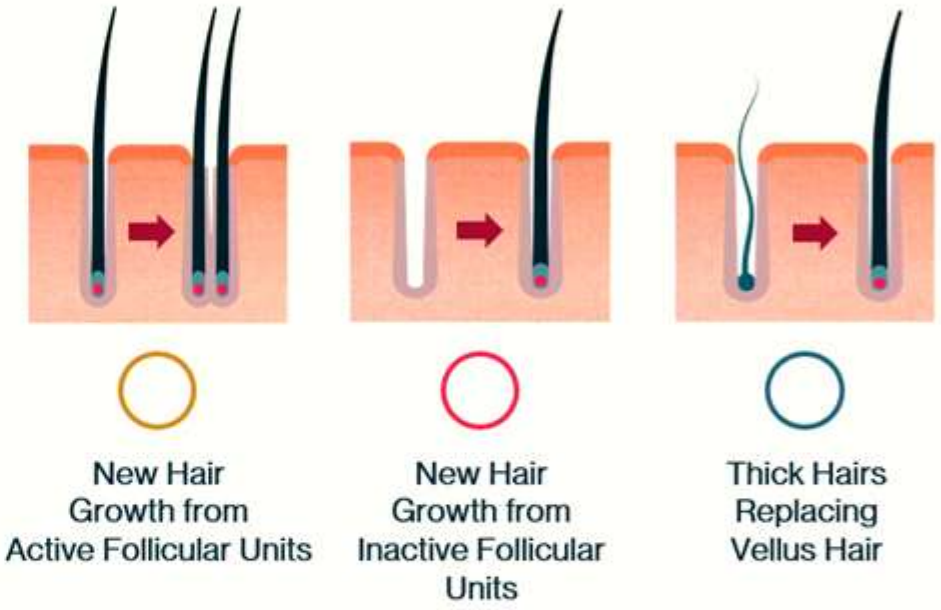
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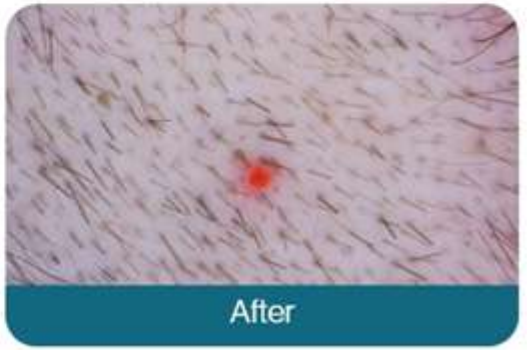

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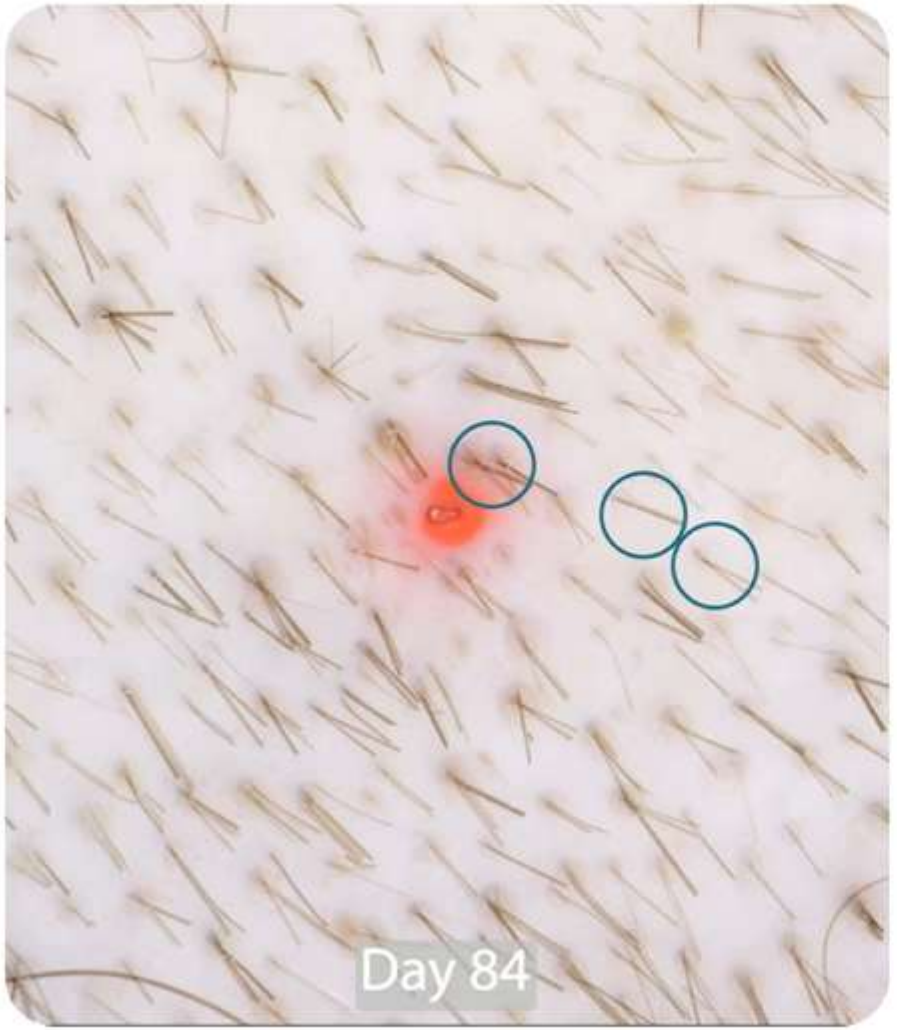

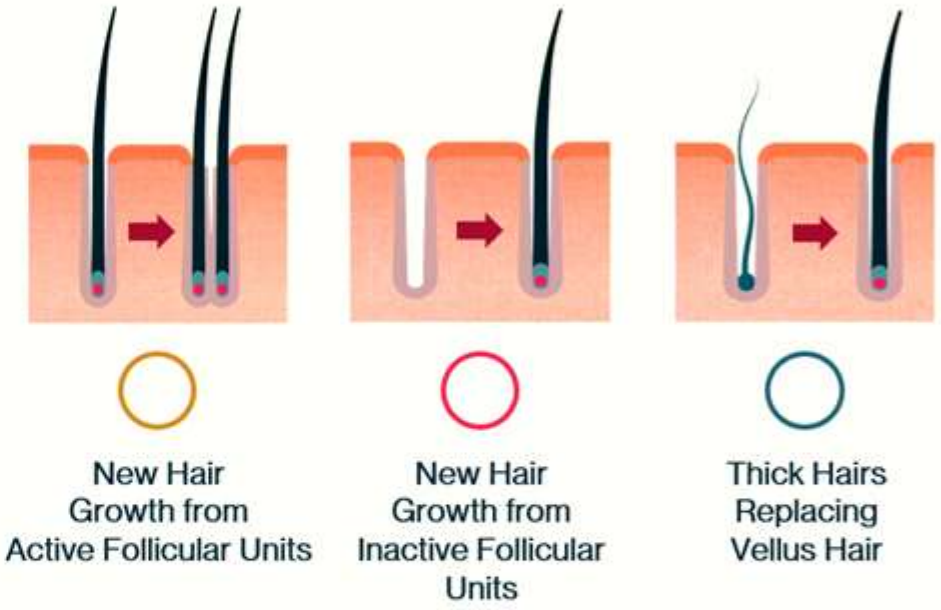
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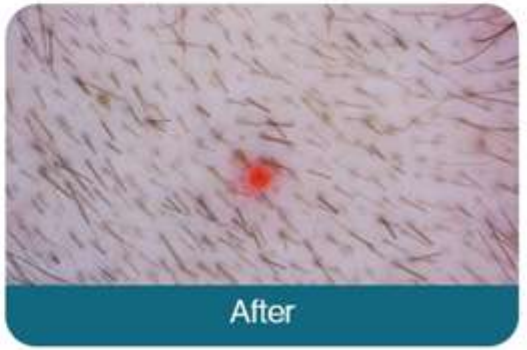

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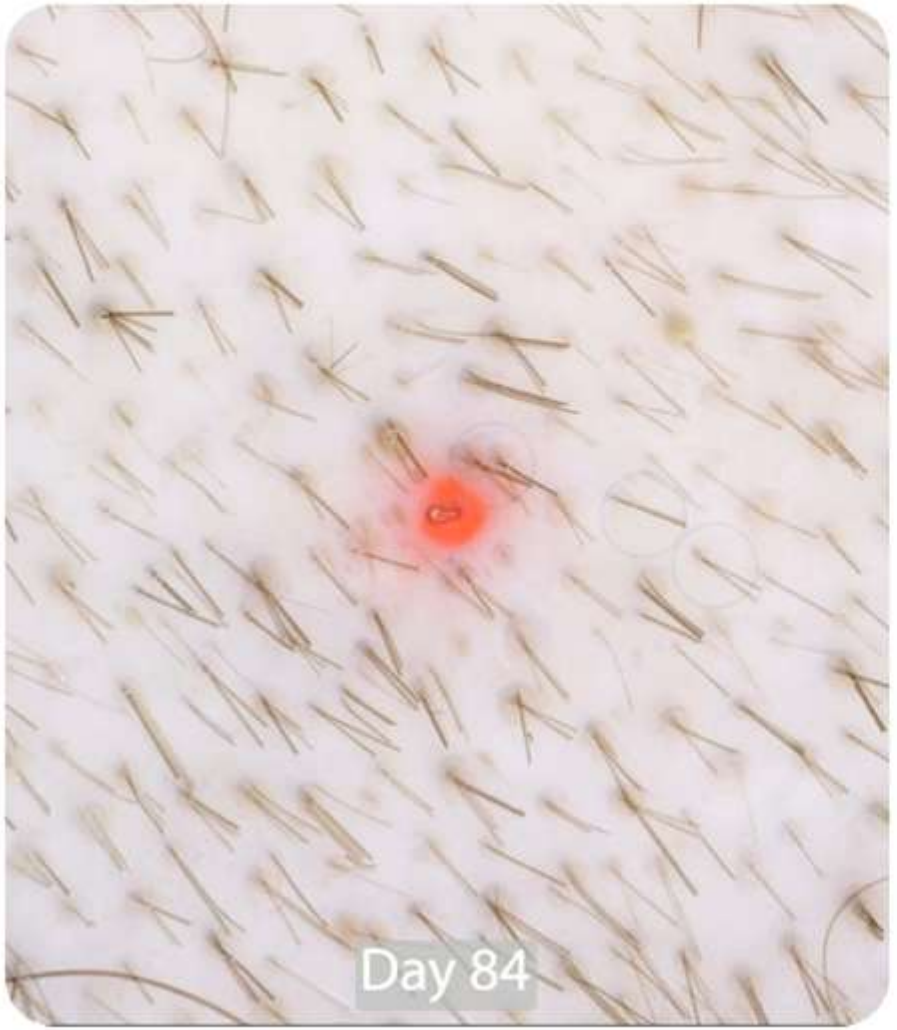

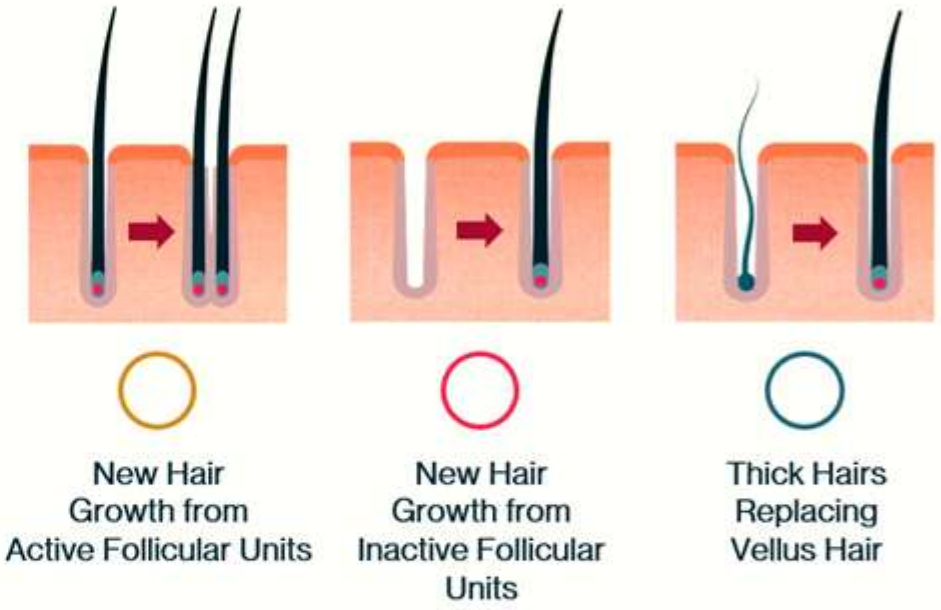
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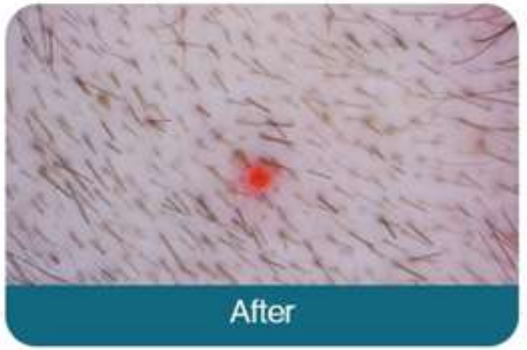
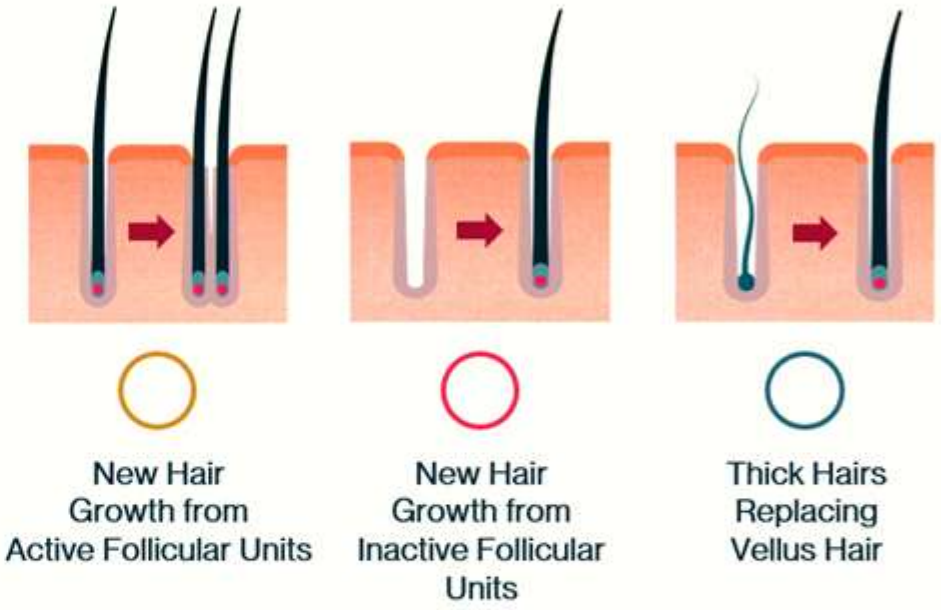


Placebo-induced hair growth differs from PP405 – macrophotography shows new growth primarily in follicular units with existing hair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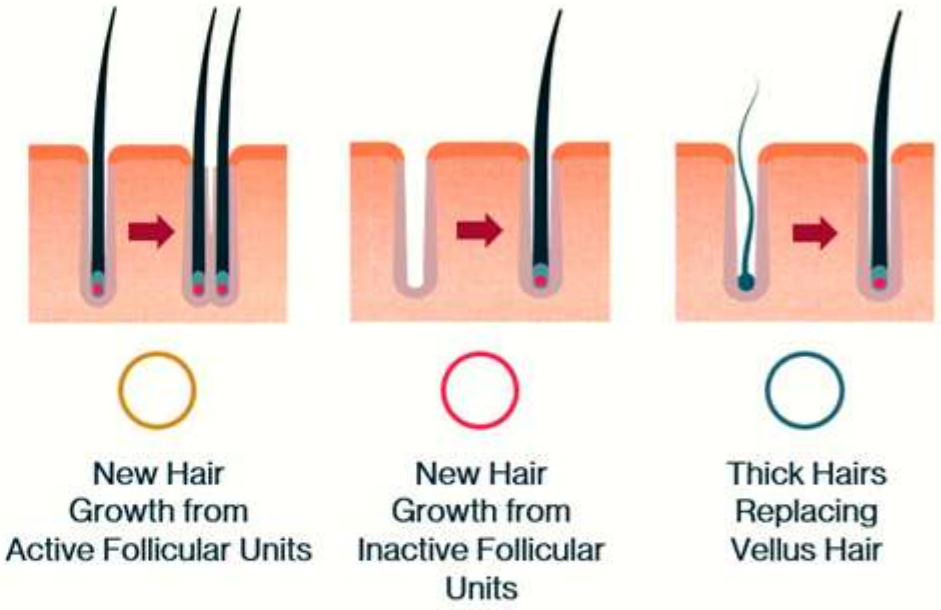
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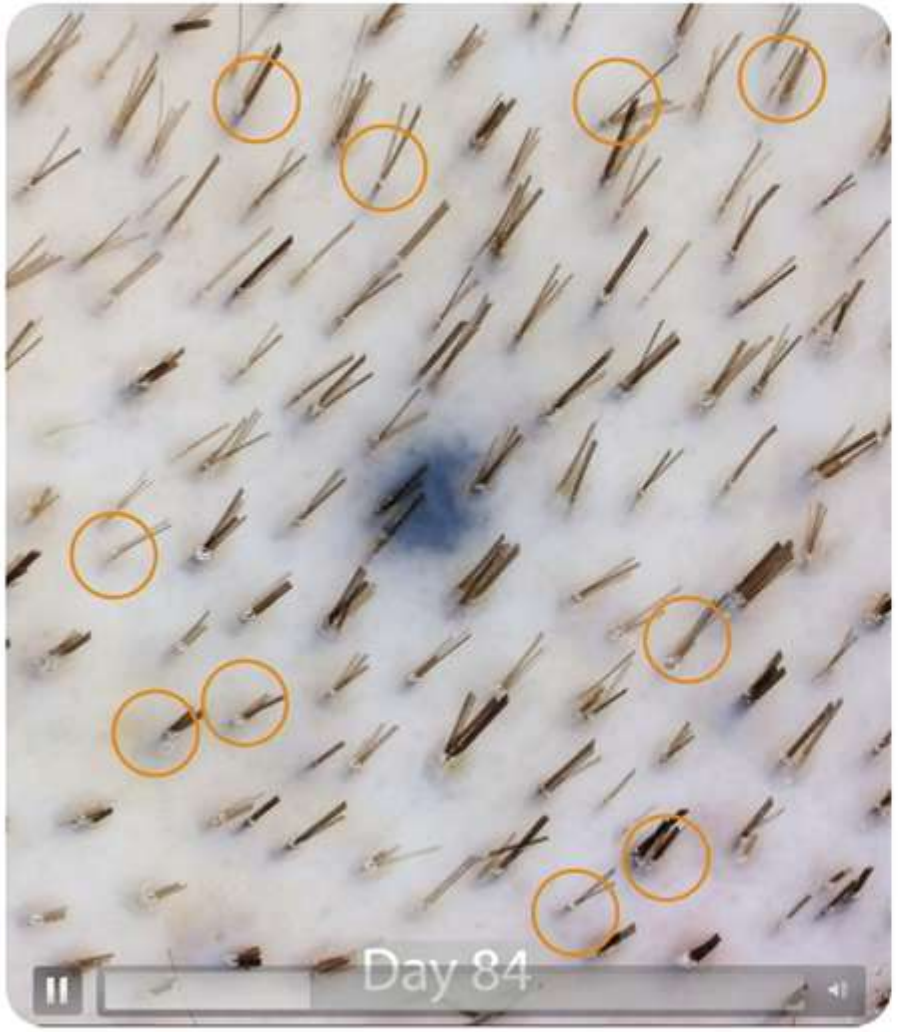

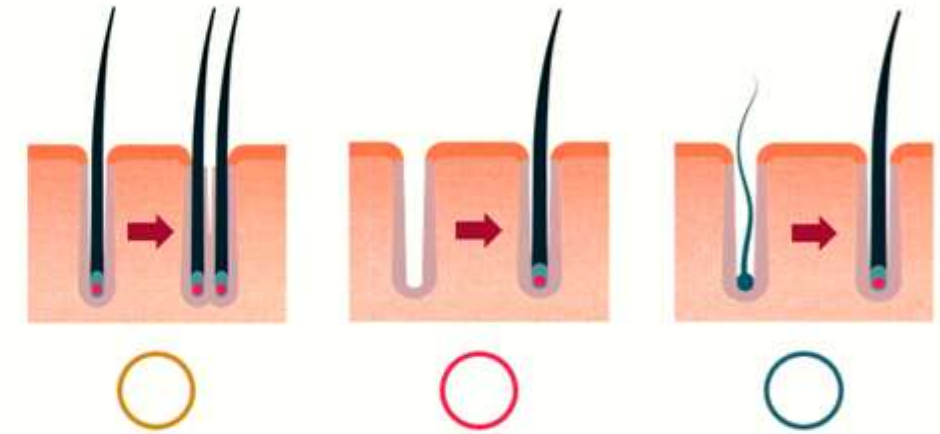
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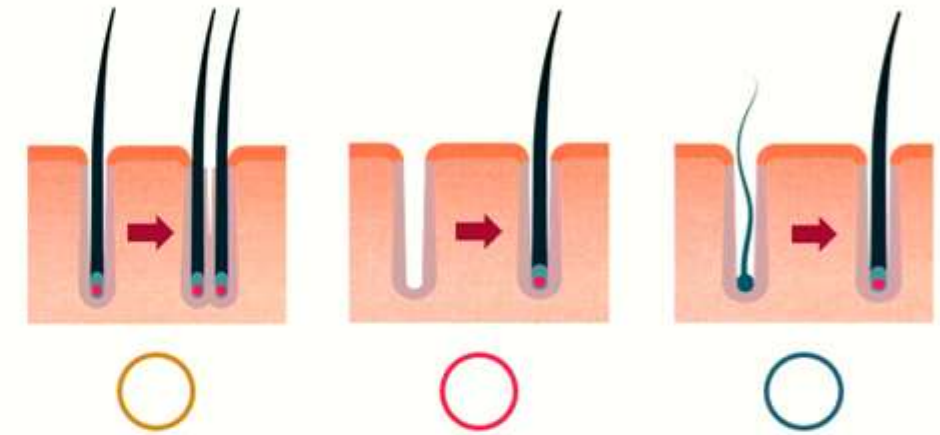
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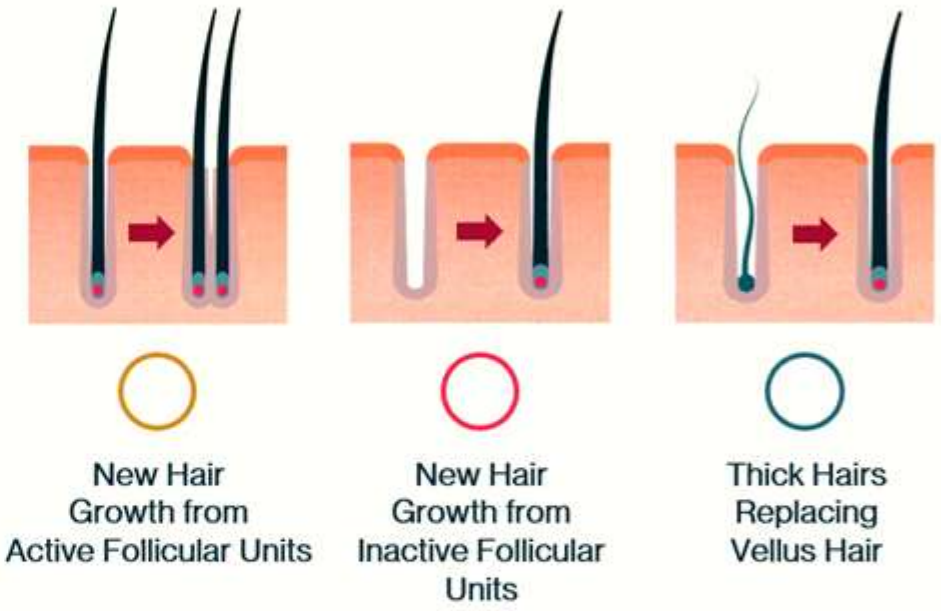
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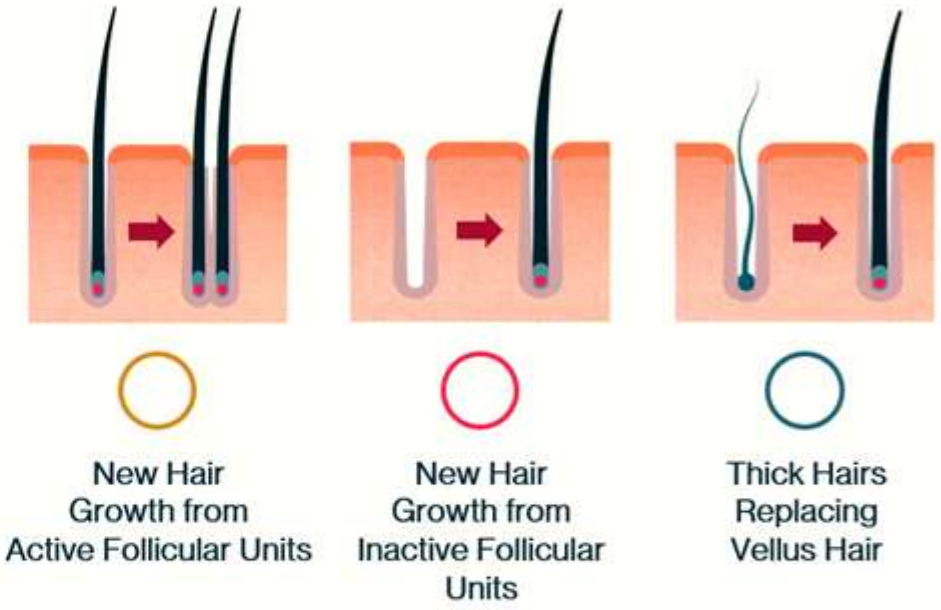
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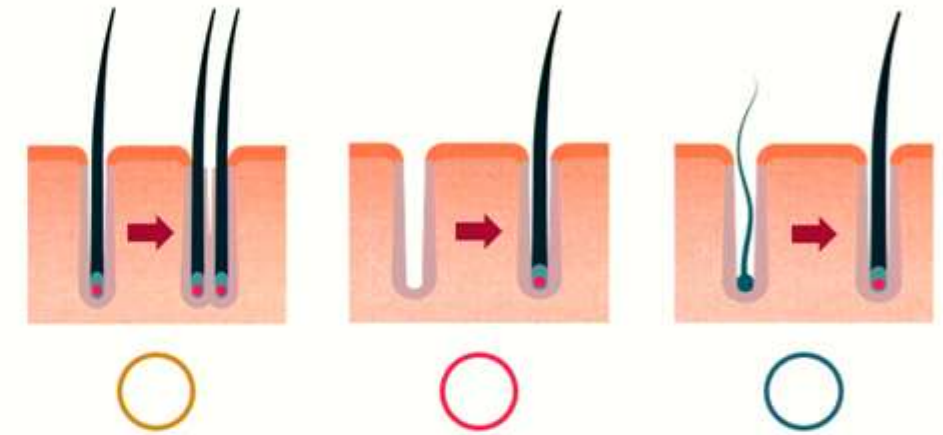
Placebo-induced hair growth differs from PP405 – macrophotography shows new growth primarily in follicular units with existing hair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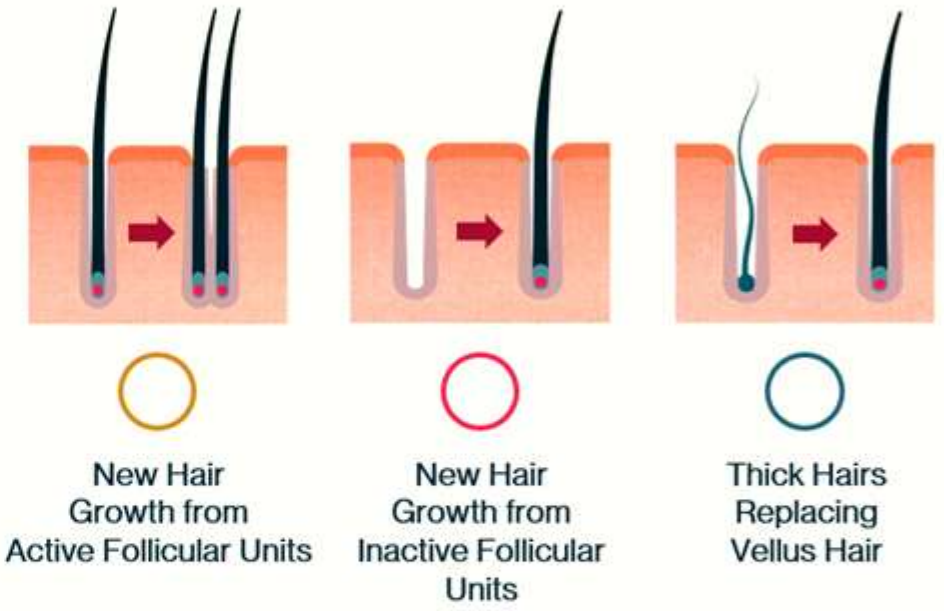
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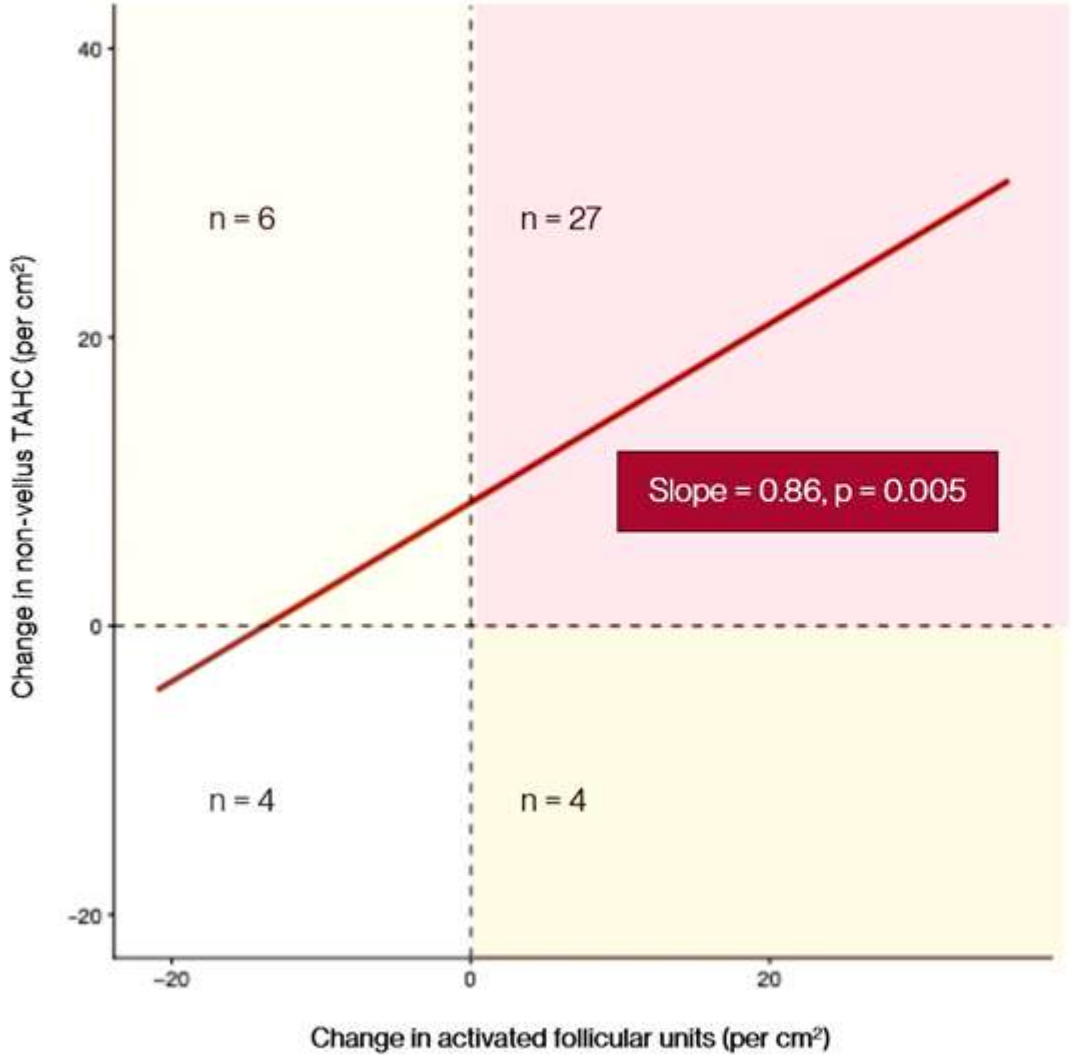
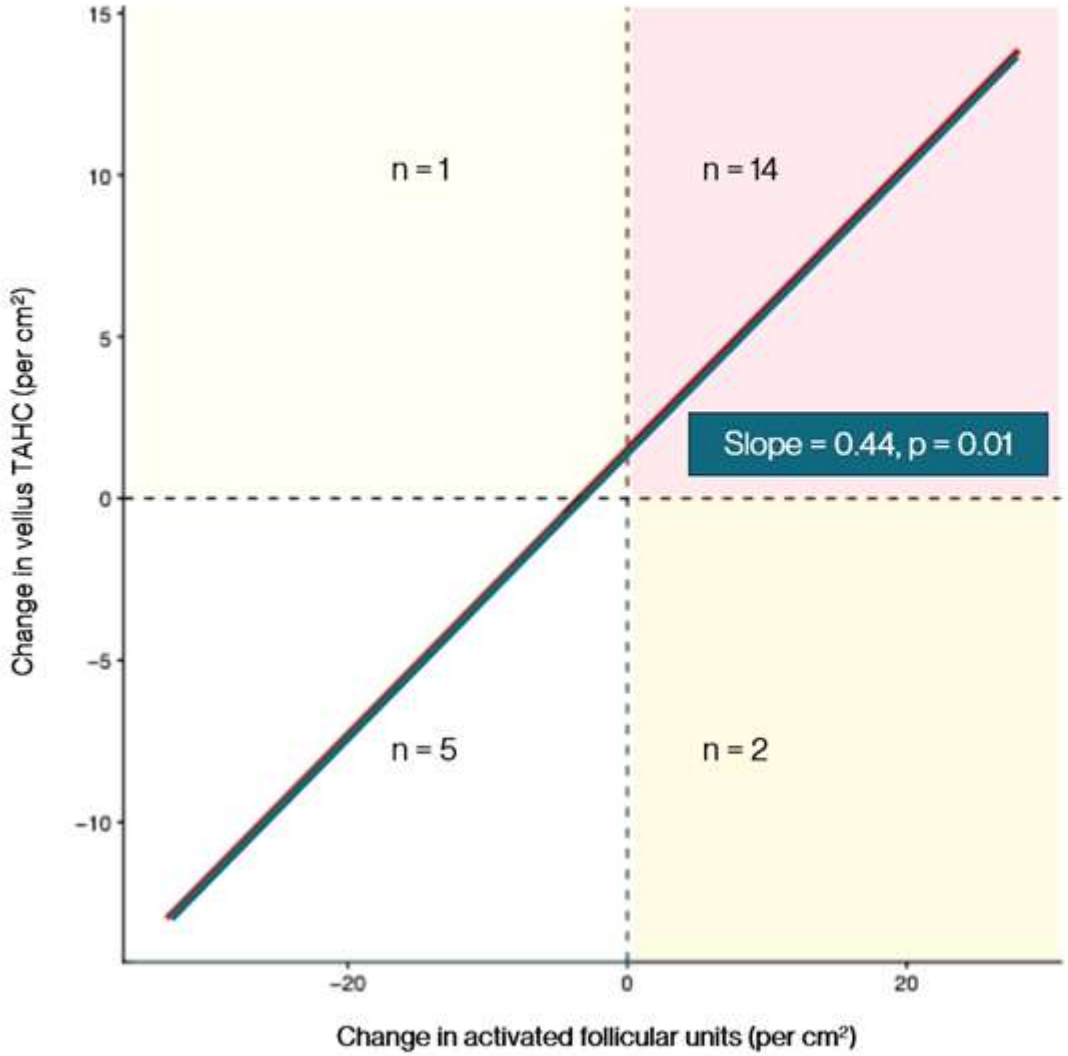
PP405-induced terminal hair growth is associated with increase of active follicular units, which is not seen on Placebo



Correlation of nvTAHC change with Follicular Unit Count change in all male subjects in the PP405 cohort in the Ph2a RCT portion (n = 41)

This correlation is not present in the placebo cohort (n = 22)
Slope = -0.017, p = 0.96

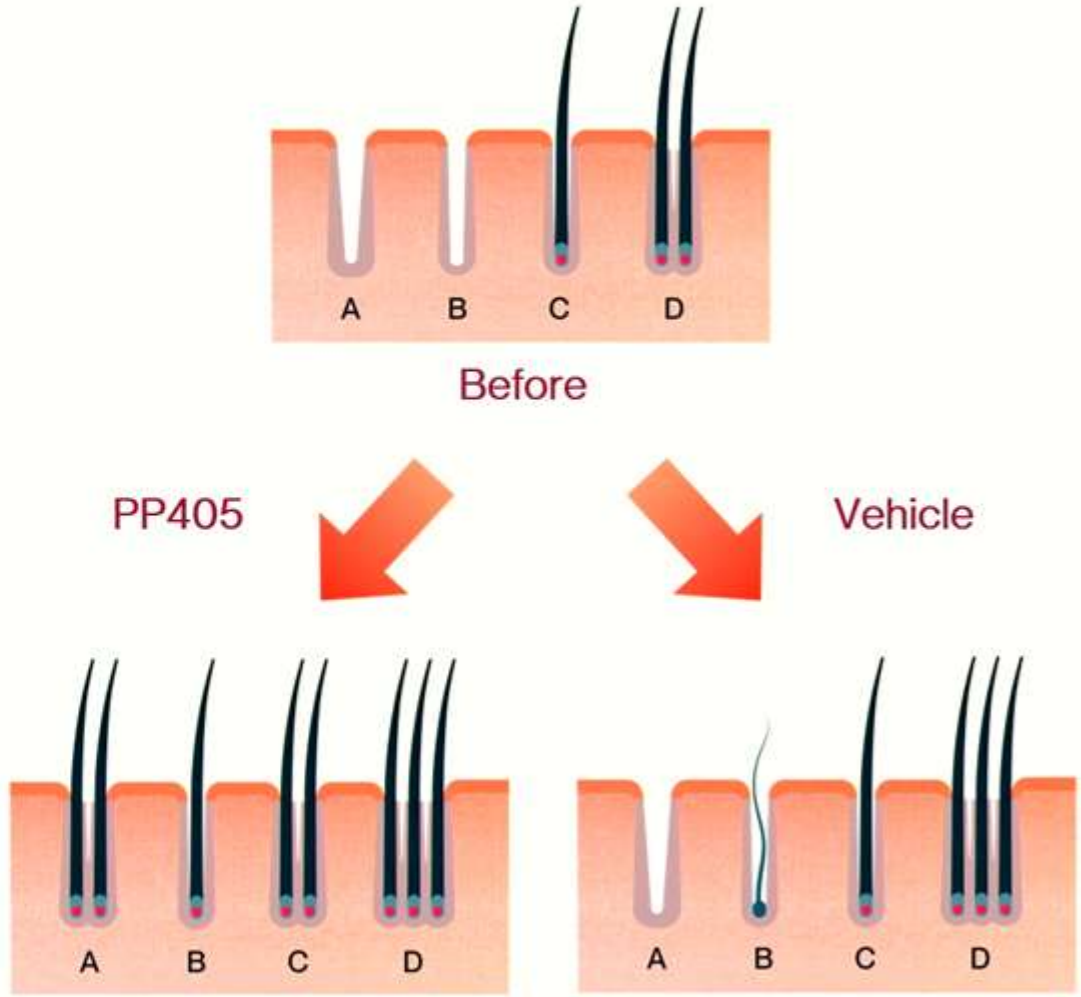
Increase in active follicular units in vehicle-treated cohort is driven by new vellus rather than terminal hair



Increased follicular units in the placebo cohort is significantly correlated with vellus hair group ($p = 0.011$)

New growth with PP405 is terminal non-vellus hair and occurs in newly activated follicular units

In addition to activating already active follicular units, PP405 drives terminal hair growth in previously dormant follicular units



Terminal hair growth stimulated by vehicle treatment is mostly in existing follicular units

Hair growth from newly activated follicular units in vehicle-treated patients tends to be vellus rather than terminal

Regeneration of hair follicles in androgenetic alopecia is possible

- PP405 drives new terminal hair growth by activating previously dormant follicular units, consistent with mechanism targeting stem cell metabolism
- Follicular Unit Count is an important endpoint for assessing novel AGA therapies by detecting newly activated follicles
- Activation of dormant follicular units in androgenetic alopecia may be possible.
- Growth of non-vellus terminal hair in previously dormant follicular units represents an important benchmark for efficacy
- Additional elaboration of efficacy and safety to be determined in upcoming clinical trials